(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
13 September 2012 (13.09.2012)

WIPO | PCT

(10) International Publication Number
WO 2012/122378 A3

(51) International Patent Classification:
C12P 21/02 (2006.01) *A61K 38/16* (2006.01)
C07K 16/28 (2006.01) *C12N 15/13* (2006.01)

(21) International Application Number:
PCT/US2012/028286

(22) International Filing Date:
8 March 2012 (08.03.2012)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
61/450,435 8 March 2011 (08.03.2011) US

(71) Applicant *(for all designated States except US)*: **THE TRUSTEES OF THE UNIVERSITY OF PENNSYLVANIA** [US/US]; 3160 Chestnut Street, Suite 200, Philadelphia, PA 19104 (US).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: **GREENE, Mark, I.** [US/US]; 300 Righters Mill Road, Penn Valley, PA 19072 (US). **ZHANG, Hongtao** [US/US]; 1651 Valley Greene Road, Paoli, PA 19301 (US).

(74) Agents: **CALDWELL, John, W.** et al.; Woodcock Washburn LLP, Cira Centre, 12th Floor, 2929 Arch Street, Philadelphia, PA 19104-2891 (US).

(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Declarations under Rule 4.17:

— *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))*

— *as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii))*

Published:

— *with international search report (Art. 21(3))*

— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))*

— *with sequence listing part of description (Rule 5.2(a))*

(88) Date of publication of the international search report:
7 November 2013

(54) Title: ANTIBODY-LIKE PROTEINS FOR THERAPEUTIC AND DIAGNOSTIC USE

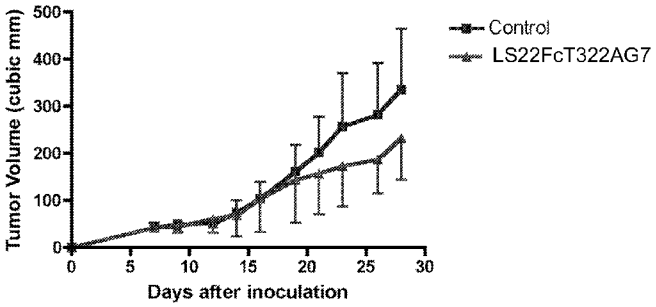


Fig. 11

(57) Abstract: Disclosed herein are recombinant protein scaffolds for use in producing antigen-binding proteins. Related antigen-binding proteins are also provided herein. In addition, nucleic acids encoding such recombinant protein scaffolds and antigen-binding proteins are also described. Vectors and cells useful for expression of the described proteins are also provided, as are methods of use.

WO 2012/122378 A3

INTERNATIONAL SEARCH REPORT

~~12/028286 05.09.2013~~

International application No.
PCT/US12/28286

A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - C12P 21/02; C07K 16/28; A61K 38/16; C12N 15/13 (2013.01)

USPC - 435/69.1; 530/387.3, 391.7; 424/134.1, 172.1, 178.1

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC(8): C12P 21/02, 21/04, 21/06, 21/08, 21/00; C07K 16/00, 16/18, 16/28, 16/30, 16/46; A61K 38/00, 38/16, 39/00 (2013.01)
USPC: 435/69.1, 69.3, 69.7, 326, 328, 330 332, 334, 344, 345; 530/387.3, 387.1, 388.1, 388.15, 388.2, 388.22, 391.1, 391.5, 391.7

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

MicroPatent (US-G, US-A, EP-A, EP-B, WO, JP-bib, DE-C,B, DE-A, DE-T, DE-U, GB-A, FR-A); Google; Google Scholar; DialogPRO; PubMed; 's22,' 's-22,' loop, cystine, cysteine, knot, antigen, bind, recombinant, heavy chain, constant domain, 'ch2,' 'ch3,' 'Fc,' 'scFc,' fragment, peptide, protein, 'ERBB2,' 'ERBB-2,' 'CD340,' 'HER-2,' 'HER-2/neu,' 'HER2,' 'p185'

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y --- A	US 7662374 B2 (GREENE, MI et al.), February 16, 2010; column 4, lines 30-38; column 5, lines 43-49; column 10, lines 41-46; column 10, lines 55-61	1, 2, 3/1, 3/2 ----- 10
Y --- A	US 2005/0202534 A1 (LEDBETTER, J et al.), September 15, 2005; abstract; paragraphs [0006], [0013], [0024], [0025]	2, 3/1, 3/2 ----- 10
A	US 6949245 B1 (SLIWKOWSKI, M), September 27, 2005; abstract; column 5, lines 16-20; column 7, lines 23-34; column 8, lines 66-67 to column 9, lines 1-6; column 9, lines 28-33; column 10, lines 9-21; column 11, lines 33-49	10
A	DIAZ-ARAYA, CM, et al. Dendritic Cells And Macrophages In Fetal Cornea. Investigative Ophthalmology & Visual Science. March 1995, Vol. 36, No. 3, pp 644-656.	1, 2, 3/1, 3/2

☐ Further documents are listed in the continuation of Box C. ☐

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
15 August 2013 (15.08.2013)	05 SEP 2013
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-3201	Authorized officer: Shane Thomas PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774

INTERNATIONAL SEARCH REPORT

~~012/028286 05.09.2013~~

International application No.
PCT/US12/28286

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☒ Claims Nos.: 4-9, 13-26
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

-***-Please See Supplemental Page-***-

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of additional fees.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Groups I+: Claims 1, 2, 3/1, 3/2, 10, SEQ ID NO: 1

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

☐ No protest accompanied the payment of additional search fees.

-Continued from Box No. III: Observations Where Unity of Invention Is Lacking:

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Groups I+: Claims 1, 2, 3/1, 3/2, 10, SEQ ID NO: 1 are directed toward a recombinant antigen-binding protein, comprising an S22 antigen-specific peptide and a CH2 region of an antibody.

Group II: Claims 11 and 12 are directed toward a recombinant antigen-binding protein comprising the protein scaffold of SEQ ID NO: 14, 16, 17, 18, 19, or 20.

SEQ ID NO: 1 will be searched without the payment of additional search fees. Additional SEQ ID NOs can be searched upon the payment of additional fees. An Exemplary Election would be: SEQ ID NO: 14. Failure to clearly identify how any paid additional invention fees are to be applied to the "+" group(s) will result in only the first claimed invention to be searched/examined.

Groups I+-II share the technical features including a recombinant antigen-binding protein, comprising an S22 antigen-specific peptide and a CH2 region of an antiboy.

However, these shared technical features are previously disclosed by the combination of US 2005/0202534 A1 to Ledbetter, et al. (hereinafter 'Ledbetter') and the article entitled 'Immunohistochemical And Topographic Studies Of Dendtritic Cells And Macrophages In Human Fetal Cornea' by Diaz-Araya, et al. (hereinafter 'Diaz-Araya'). Ledbetter discloses a recombinant antigen-binding protein (abstract; recombinantly produced binding domain-immunoglobulin fusion proteins that feature a binding domain for a cognate structure such as an antigen), comprising an antigen-specific peptide (abstract; binding domain-immunoglobuling fusion proteins that features a binding domain for a cognate structure such as an antigen) and a CH2 region of an antibody (abstract; and immunoglobulin CH2 and CH3 domains). Ledbetter does not disclose an S22 antigen-specific peptide. Diaz-Araya does disclose the study of morphologic forms of S22-positive immunoreactive macrophage cells (abstract; page 644). It would have been obvious to a person of ordinary skill in the art, at the time of the invention, to integrate the use of an S22 antigen-specific peptide within the previous disclosure of the use of a recombinant antigen-binding protein, comprising an antigen-specific peptide and a CH2 region of an antibody, by Ledbetter, and provide the previously disclosed antigen-specific peptide as being an S22 antigen-specific peptide for utility in various ocular, ophthalmic and corneal applications (Diaz-Araya; abstract; page 644), including the diagnosis and treatment of ocular and other types of cancer, as S22 antigen-presenting cells can be associated with such tissue types (Diaz-Araya; abstract; page 644).

Since none of the special technical features of the Groups I+-II inventions is found in more than one of the inventions, and since all of the shared technical features are previously disclosed by the combination of the Ledbetter and Diaz-Araya inventions, unity of invention is lacking.